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Inefficiency of insulin therapy to correct apolipoprotein A-I metabolic abnormalities in non-insulin-dependent diabetes mellitus.

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Non-insulin-dependent diabetes mellitus (NIDDM) is associated with low high density lipoprotein (HDL) cholesterol and apoA-I, related to an increased apoA-I fractional catabolic rate. This stable isotope kinetic experiment, using L-[1-(13)C] leucine, was designed to study the effect of insulin therapy on HDL apoA-I and A-II metabolism in poorly controlled NIDDM patients. A kinetic study was performed in five control subjects and in six NIDDM patients before and two months after the introduction of insulin therapy. ApoA-I and A-II were modelled using a monoexponential function. Insulin treatment was able to correct neither the low HDL apoA-I concentration observed in NIDDM patients (1.14+/-0.19 vs. 1.16+/-0. 12 g l (-1) (controls: 1.33+/-0.14)), nor the HDL apoA-I hypercatabolism (0.39+/-0.11 vs. 0.34+/-0.05 pool d(-1), (controls: 0.23+/-0.01, P< 0.01)). HDL apoA-I production rate was increased in NIDDM patients compared to control subjects and was not modified by insulin (0.45+/-0.12 vs. 0.39+/-0.08 g d(-1) l(-1), (controls: 0. 31+/-0.04, P< 0.05)). HDL apoA-II kinetic parameters were initially not significantly different between NIDDM patients and control subjects, and were not modified by insulin. The decreased insulin sensitivity, assessed by the insulin suppressive test, was not modified by insulin therapy in NIDDM patients. HDL apoA-I fractional catabolic rate was significantly correlated to HDL triglyceride/cholesteryl ester and triglyceride/protein ratios, which were significantly higher in NIDDM patients than in controls and were not modified by insulin therapy. The persistence of insulin resistance and of high neutral lipid exchanges between triglyceride rich lipoproteins and HDL in insulin-treated NIDDM

patients probably explain the inefficiency of insulin therapy to correct HDL apoA-I metabolic abnormalities.

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